

**REMARKS**

**A. The Amendments and the Status of the Claims**

Claims 100, 127, and 412 have been amended to define the Applicants' invention with more precision and particularity. The claims, as amended, are supported by the specification and the original claims. No new matter has been added. Claims 1-99, 101, 103-126, 128-193, 201, 202, 204-209, 214-216, 229-293, 301, 302, 304-309, 330, 338-346, and 357-411 have been previously canceled without prejudice. Claims 100, 102, 127, 194-200, 203, 210-213, 217-228, 294-300, 303, 310-329, 331-337, 347-356, and 412 are pending.

**B. Priority**

The Examiner has repeated the previous assertion that the effective priority date of the present application is May 1, 1996 (second full paragraph on page 2 of the Office Action). Accordingly, the Applicants' contention that May 1, 1996 is an incorrect priority date has been disregarded by the Examiner. As a result, the Examiner refused to accord the present application what the Applicants believe is the correct priority date of June 7, 1995. The Examiner's position remains that the present application is only entitled to the benefit of its own filing date, because the parent application allegedly does not satisfy the written description requirement of 35 U.S.C. § 112, paragraph 1, as the written description requirement relates to the currently pending claims.

The Applicants maintain their previous position with respect to the correct priority date stated above and respectfully disagree with the Examiner. Indeed, previously the Applicants have demonstrated that every limitation of the claims of this continuation-in-part application is disclosed in the parent application in such a way as to satisfy the requirements of 35 U.S.C. § 112.

More specifically, previously the Applicants have stated that every feature, element, limitation, and relationship between them recited in the currently pending claims are adequately disclosed in the parent application and have explained why. The Applicants explained why the parent application provides enough information to lend more than sufficient support to the claimed formulations, including a detailed description of the claimed gas species in combination with the specific phospholipids, gas mixtures, linking groups of polymeric moiety covalently bound to the phospholipids and targeting ligand of proteins, peptides, and steroids.

Indeed, the instant claims recite compositions that include gas-filled vesicles, where the gas is a perfluorocarbon or sulfur hexafluoride, where the vesicles include a disulfide linkages-free phospholipid, covalently conjugated to a targeting ligand via a linking group. The Applicants previously have provided a very detailed analysis showing that the parent application unambiguously teaches that the Applicants were in possession of such vesicles (page 8, lines 4-5 of the parent application) filled with a gas (page 15, lines 14-15). Both perfluorocarbons and sulfur hexafluoride are also (page 16, lines 8-9 and claim 6). Use of phospholipids is also disclosed (page 9, lines 16-17), as well as use of disulfide-free linkages (i.e., amide, ester, thioester, ether, or amino linkages, page 48, lines 20-24 and lines 34-36).

With respect to using linking group is a hydrophilic polymer such as PEG, polypropylene glycol, polyvinylalcohol, polyvinylpyrrolidone, and copolymers thereof as a linking moiety, using such polymers is also disclosed (page 38, line 21, hydrophilic polymers generally; page 37, line 37 through page 38, line 8, specific hydrophilic polymers). Finally, the instant claims require the presence of lipid-linking group-targeting ligands, such as proteins, peptides, saccharides, steroids, steroid analogs, bioactive agents and genetic material. Such features are also disclosed (page 48, lines 12-18 a lipid-linking group-targeting ligand; page 8, lines 9-15 and page 43, line 10 through page 44, line 18, specific ligands).

It is, therefore, abundantly clear that the instant claims are sufficiently and adequately supported by the written description of the parent application. Unfortunately, the Examiner ignores the arguments and analysis advanced by the Applicants in the previous response and summarily rejected these arguments calling them "not persuasive" (page 9, Response to Argument portion of the Office Action). The Examiner has stated no reasons or explanation why any of the Applicants' arguments are incorrect. The Examiner just vaguely referred to the reasons stated in the Office Action mailed December 28, 2005. The Applicants respectfully submit that this is not enough. The previous response addressed the reasons for denial of priority as stated in December 28, 2005, Office Action, and the Applicants have a right to have their arguments considered and not rejected without any explanation.

The Applicant further respectfully submit that the rules require an examiner to provide a reasoned statement, and when a rejection is traversed, as here, the examiner is required, if the rejection is repeated, to take note of the applicant's argument and to answer the substance of it. See, MPEP § 707.07(f). In this case, the Applicants argued, traversing a previous rejection, that the present application has the priority date June 7, 1995. However, the Examiner summarily rejected this argument by simply repeating the language found in a previous Office Action and has failed to explain why the argument was not persuasive. The Applicants respectfully submit that such treatment is improper and contradicts the rules promulgated by the MPEP.

In view of the foregoing, the Applicants' position remains that the claims of the present application are fully supported by the disclosure of the parent application. Accordingly, it is submitted that the present continuation-in-part application is entitled to the priority date of the parent application, i.e., June 7, 1995. Reconsideration of the denial of this priority date is respectfully requested.

**C. Rejections Under 35 U.S.C. § 103(a)**

Claims 100, 102, 127, 194-200, 203, 210-213, 217-220, 294-300, 303, 310-317, 326, and 412 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over U.S. Patent No. 5,620,689 to Allen ("Allen"), in view of U.S. Patent No. 4,853,228 to Wallach ("Wallach"), U.S. Patent No. 5,643,553 to Schneider ("Schneider") and U.S. Patent No. 5,648,098 to Porter ("Porter") (page 3, first paragraph of the Office Action). In addition, claims 318-325, 327-329, 331-337, and 347-356 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Allen, in view of Wallach, Schneider and Porter and further in view of U.S. patent No. 5,656,442 to Ginsburg ("Ginsburg") (page 5, last paragraph of the Office Action). These rejections are respectfully traversed.

The basic criteria that must be satisfied to establish a *prima facie* case of obviousness were discussed previously (see the response to a previous Office Action filed 09/28/05). The Applicants respectfully submit that these criteria have not been satisfied in this case because none of the cited references, either alone or in combination, disclose or suggest every limitation of claims 100, 127, and 412.

More specifically, the combinations of art set forth by the Examiner require the use of Porter, the disclosure of which teaches the use of perfluorocarbons. Each of other references, or a combination thereof are silent with respect to the use of perfluorocarbons, and, clearly, without the use of perfluorocarbons none of the cited references nor any combination thereof, meets or suggests every limitation of claims 100, 127, and 412. However, in view of the above discussion on the issue of priority, Porter is not available as the proper prior art reference, because the earliest reference date for Porter is only October 17, 1995. Therefore, the present application pre-dates Porter, and accordingly Porter is not prior art against the present application, and does not qualify as a valid 35 U.S.C. § 103 reference.

Even if Porter were available as a prior art reference, the Applicants submit that the modification of Schneider as proposed by the Examiner would be improper because there is nothing in Schneider, or in Allen, Wallach, or Ginsburg, or in any combination of these four references providing suggestion that might motivate one skilled in the art to prepare such formulation. These references are simply silent in that regard.

Specifically, each of claims 100, 127, and 412, now recites vesicles including a solid state membrane. Schneider fails to disclose or suggest the vesicles having a solid state membrane encompassing a gas. All that is disclosed by Schneider is microbubbles having the gas/liquid interface. A solid state membrane cannot be found anywhere in Schneider. None of other references cited by the Examiner can cure this deficiency of Schneider. Indeed, there is no suggestion or motivation in any of Wallach, Allen and Porter to modify what is described in Schneider so as to arrive to the solid state membrane limitation.

Moreover, it is respectfully submitted that not only does Schneider fail to disclose or suggest the vesicles having a solid state membrane, but Schneider even teaches away from using the microcapsules having such membrane. In fact, Schneider teaches that the microcapsules having solid membrane are so different from the microbubbles (having no such solid membrane) that they "belong to a different kind of art" (Col. 3, line 41). Schneider is concerned exclusively with the microbubbles without the solid state membrane and teaches or suggest nothing beyond such embodiments.

It is, therefore, clear that Schneider, alone or in combination with Wallach, Allen, and Porter, neither teaches nor suggests using the gas-filled vesicles having a solid state membrane as required by claims 100, 127, and 412 as now amended.

With respect to the second obviousness rejection, Ginsburg fails to cure the above-discussed deficiencies of combination of Schneider Wallach, Allen, and Porter. Indeed, Ginsburg only teaches specific targeting agents. There is nothing in Ginsburg that could conceivably motivate one having ordinary skill in the art to modify Schneider

to use solid state membranes. Ginsburg does not even teach or suggest using any kind of gas-filled vesicles.

Accordingly, it is respectfully submitted that claims 100, 127 and 412 are patentably distinguishable over the combination of Wallach, Allen, Schneider, and Porter or over the combination of Wallach, Allen, Schneider, Porter, and Ginsburg cited by the Examiner. All other claims depend, directly or indirectly, on either claim 100 or claim 127, and are allowable for at least the same reason. Reconsideration and withdrawal of the rejection are respectfully requested.

**E. Double Patenting Rejection**

Claim 100 stands rejected under the non-statutory, judicially created doctrine of obviousness-type double patenting over claims 1-58 of U.S. Patent No. 6,521,211 (page 7, fourth paragraph of the Office Action).

In addition, claims 100, and 194-200 also stand provisionally rejected under the non-statutory, judicially created doctrine of obviousness-type double patenting over claims 73, 76, and 101-112 of co-pending U.S. Patent Application No. 10/341,167 (page 8, second paragraph of the Office Action).

While the Applicants respectfully traverse this rejection, it is believed that this issue has become moot in view of the terminal disclaimer which accompanies this response. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

In re Application of:  
Unger et al.  
Application No.: 09/218,660  
Filed: December 22, 1998  
Page 19

PATENT  
Attorney Docket No.: IMARX1100-3

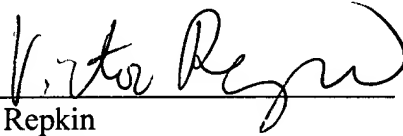
### CONCLUSION

In view of the above amendments and remarks, reconsideration and favorable action on all claims are respectfully requested. In the event any matters remain to be resolved, the Examiner is requested to contact the undersigned at the telephone number given below so that a prompt disposition of this application can be achieved.

Check number 585111 in the amount of \$65.00 is enclosed as payment for the Terminal Disclaimer filing fee. No other fee is believed to be due in connection with filing this submission. However, the Commissioner is hereby authorized to charge any other fees associated with the filing submitted herewith, or credit any overpayments to Deposit Account No. 07-1896 referencing the above-identified attorney docket number. A copy of the Transmittal sheet is enclosed.

Respectfully submitted,

Date: March 19, 2007

  
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